

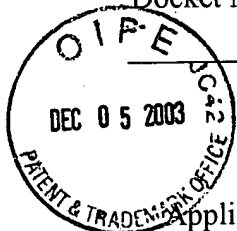
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Docket No.: VANMA48.001CP1

Customer No: 20,995

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1644

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TECH CENTER 16.03/2003



### AMENDMENT / RESPONSE TRANSMITTAL

Applicant : Laub, et al.  
App. No. : 09/853,080  
Filed : May 9, 2001  
For : ANTIGENIC POLYPEPTIDE  
SEQUENCES OF FACTOR  
VIII, AND FRAGMENTS  
AND/OR EPITOPES OF  
THESE SEQUENCES  
Examiner : Nolan, Patrick J.  
Art Unit : 1644

#### CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

December 3, 2003

(Date)

Maria L. Gordey, Reg. No. 52,950

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Transmitted herewith for filing in the above-identified application are the following enclosures:

- (X) Amendment and Response to Restriction Requirement in 7 pages.
- (X) Substitute Sequence Submission Statement.
- (X) Sequence Listing (paper copy) in 18 pages.
- (X) Sequence Listing on diskette.

The fee has been calculated as shown below:

FEE CALCULATION				
FEE TYPE		FEE CODE	CALCULATION	TOTAL
Total Claims	14 - 41 = 0	1202 (\$18)	0 x 18 =	\$0
Independent Claims	3 - 12 = 0	1201 (\$86)	0 x 86 =	\$0
Multiple Claim		1203 (\$290)	PREVIOUSLY PAID	\$0
5 Month Extension		1255 (\$2,010)		\$2,010
			<b>TOTAL FEE DUE</b>	<b>\$2,010</b>

- (X) An extension of time is hereby requested by payment of the appropriate fee indicated above.
- (X) A check in the amount of \$2,010 is enclosed.

- (X) Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

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Marina L. Gordey  
Registration No. 52,950  
Agent of Record  
Customer No. 20,995  
(805) 547-5580



MA48.001CP1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant : Laub, et al.  
Appl. No. : 09/853,080  
Filed : May 9, 2001  
For : ANTIGENIC POLYPEPTIDE  
SEQUENCES OF FACTOR VIII,  
FRAGMENTS AND/OR EPITOPES  
OF THESE SEQUENCES  
Examiner : Nolan, Patrick J.  
Group Art Unit : 1644

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In response to the Restriction Requirement mailed June 3, 2003, please amend the above-identified application as follows:

**Amendments to the Specification** begin on page 2 of this paper.

**Amendments to the Sequence Listing** begin on page 3 of this paper.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 4 of this paper.

**Remarks/Arguments** begin on page 7 of this paper.

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Appl. No. : 09/853,080  
Filed : May 9, 2001

### AMENDMENTS TO THE SPECIFICATION

**Please replace the paragraph starting on page 16, lines 27-29 with the following paragraph:**

The present invention relates to the antigenic polypeptide sequences of factor VIII and/or fragments of these sequences, as described by ~~Verhar~~ Vehar et al. (1984) (SEQ ID NO: 49).

**Please replace the paragraph starting on page 17, lines 10-15 with the following paragraph:**

A first embodiment of the invention relates to the antigenic polypeptide sequence A3 of factor VIII, and to fragments and/or epitopes of this sequence. The said sequence contains the fragments glutamic acid 1649 to histidine 2031 inclusive, arginine 1652 to arginine 1917 inclusive or arginine 1803 to arginine 1917 inclusive, of the polypeptide sequence (SEQ ID NO: 49) of factor VIII as published by ~~Verhar~~ Vehar et al. (1984) and Toole et al. (1984).

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**Filed** : **May 9, 2001**

### **AMENDMENTS TO THE SEQUENCE LISTING**

Please replace the original Sequence Listing with the accompanying Substitute Sequence Listing. Support for the amendment can be found in the deduced Factor VIII amino acid sequence as published in Vehar et al. 1984 Nature 312, pp. 337-342 referred to in the Specification as filed on page 16, line 28, and now presented as **SEQ ID NO: 49**. Therefore, no new matter has been introduced with these amendments.

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Filed : May 9, 2001

### AMENDMENTS TO THE CLAIMS

Restriction to one of the following groups was required under 35 U.S.C. 121:

- Group I. Claims 1-15, 20-23, drawn to peptide from Factor VIII, classified in class 530, subclass 300.
- Group II. Claims 16-17, 20-23, drawn to antibodies to Factor VIII, classified in class 530, subclass 387.1.
- Group III. Claims 18-23, drawn to anti-Id antibodies, classified in class 530, subclass 387.2.
- Groups IV or V or VI. Claims 24 and 26, drawn to a method of *in vivo* treatment with the products of Groups I-III, classified in class 424, subclass 130.1, 131.1 and class 514, subclass 13.
- Groups VII or VIII or IX. Claim 25 drawn to a method *ex vivo* blood treatment with the products of Groups I-III, classified in class 424, subclass 140.1
- Groups X or XI or XII. Claims 27-28, drawn to a method of identifying inhibitors with the products of Groups I-III, classified in class 435 subclass 4.

In response to the restriction requirement, Applicant provisionally elects Group I, that is, Claims 1-15 and 20-23. In addition, Applicant elects species of SEQ ID NO: 30. Claims 1-28 have been canceled without prejudice. The Applicant reserves the right to pursue the subject matter of the canceled claims in a related application. New claims 29-41 have been added.

New Claims 29-33 are similar to now canceled Claims 1-28 and reflect the Applicant's election of the species of SEQ ID NO: 30. However, the Applicant respectfully requests that the Examiner also considers new Claims 34-41. These claims are drawn to domain C of factor VIII and to the subfragments of said domain. The position of domain C is known in the art as amino acid residues 2020-2172 and 2173-2332 (see Foster et al., 1990, cited on page 1, line 31 of the Specification as filed). Therefore, support for the new claims 34-39 can be found in the Specification as originally filed (also, for example, on page 21, lines 23 through page 24, line 1). Therefore, no new matter has been introduced herewith.

**Please cancel Claims 1-28 without prejudice.**

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**Please add the following new Claims:**

29. (New) An isolated or purified polypeptide comprising an epitope of factor VIII, wherein said epitope is the epitope isoleucine 2262 to glutamine 2270 inclusive, defined by the following sequence: Ile Ser Ser Ser Gln Asp Gly His Gln of SEQ ID NO: 30.
30. (New) A pharmaceutical composition comprising an adequate pharmaceutical carrier and the polypeptide of Claim 29.
31. (New) A diagnostic and/or purification device, which comprises at least one element selected from the group consisting of factor VIII, and the polypeptide of Claim 29.
32. (New) The device according to Claim 31, wherein said device is a diagnostic kit.
33. (New) The device according to Claim 31, wherein said device is a chromatography column or filter.
34. (New) An isolated or purified polypeptide comprising an epitope of factor VIII, wherein said epitope is the polypeptide sequence C of factor VIII protein of SEQ ID NO: 49.
35. (New) An isolated or purified antigenic sequence, selected from the group consisting of the following fragments of factor VIII polypeptide of SEQ ID NO: 49:
- a) a sequence starting from isoleucine 2242 to tyrosine 2332 inclusive;
  - b) a sequence starting from isoleucine 2242 to tyrosine 2305 inclusive;
  - c) the sequence of (b), wherein one or more amino acids of the terminal peptide Thr-Arg-Tyr are deleted;
  - d) a sequence starting from isoleucine 2262 to serine 2289 inclusive;
  - e) a sequence starting from leucine 2273 to tyrosine 2332 inclusive;
  - f) a sequence starting from leucine 2273 to tyrosine 2305 inclusive;
  - g) the sequence of (g), wherein one or more amino acids of the terminal peptide Thr-Arg-Tyr are deleted;
  - h) a sequence starting from proline 2292 to tyrosine 2332 inclusive,
- and epitopes of the sequences (a) through (i) selected from the group consisting of:
- i) an epitope glycine 2242 to leucine 2251 inclusive, defined by the following sequence: Gly Val Thr Thr Gln Gly Val Lys Ser Leu of SEQ ID NO: 29;
  - j) an epitope isoleucine 2262 to glutamine 2270 inclusive, defined by the following sequence: Ile Ser Ser Ser Gln Asp Gly His Gln of SEQ ID NO: 30;

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**Filed** : May 9, 2001

k) an epitope leucine 2273 to serine 2289 inclusive, defined by the following sequence: Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser of SEQ ID NO: 31;

l) an epitope proline 2292 to tyrosine 2305 inclusive, defined by the following sequence: Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr of SEQ ID NO: 32;

m) the epitope of (m), wherein one or more amino acids of the terminal tripeptide Thr-Arg-Tyr are deleted;

n) an epitope glutamic acid 2322 to tyrosine 2332 inclusive, defined by the following sequence: Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr of SEQ ID NO: 33; and

o) any of the preceding epitopes or sequences (a) through (n), wherein at least one amino acid has been deleted.

36. (New) A purified or isolated conformational epitope or sequence which contains at least two different epitopes or sequences according to Claim 35 and any of the preceding epitopes or sequences wherein at least one amino acid has been deleted.

37. (New) A complex comprising a carrier protein or a carrier peptide linked to the sequences or epitopes according to Claims 35 or 36.

38. (New) A pharmaceutical composition comprising an adequate pharmaceutical carrier and at least one element selected from the group consisting of domain C of factor VIII of SEQ ID NO: 49, and the antigenic fragment of Claim 35.

39. (New) A diagnostic and/or purification device, which comprises at least one element selected from the group consisting of domain C of factor VIII, and the antigenic fragment of Claim 35.

40. (New) The device according to Claim 39, wherein said device is a diagnostic kit.

41. (New) The device according to Claim 39, wherein said device is a chromatography column or filter.

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### REMARKS

The Specification has been amended to include a SEQ ID NO for the sequence of the human Factor VIII protein. Support for the amendment can be found in the Specification as filed on page 16, line 28. Therefore, no new matter has been introduced.

New claims 29-41 have been added. As a result, Claims 29-41 are pending.

The Sequence Listing has been amended. Support for the amendments can be found in the Specification as filed and in the published amino acid sequence of human Factor VIII. Therefore, no new matter has been introduced with the amendments.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 3, 2003

By: \_\_\_\_\_

Marina L. Gordey  
Registration No. 52,950  
Agent of Record  
Customer No. 20,995  
(805) 547-5586

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